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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,529	05/31/2000	Colin Collins	02307O-111900US	6021

20350 7590 09/12/2003

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EXAMINER
BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
1631	18

DATE MAILED: 09/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/586,529	COLLINS ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 10-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/23/03 has been entered.

Status of Claims

2. Claim 1 is amended. Claims 24,25 are added. Claims 1-6, 10-25 are pending.

Claim Rejections - 35 USC § 103.

3. Claims 1-6, 10-25 are rejected under 35 U.S.C. 103(a) as obvious over Brosch et al. or Kelley et al. or Roach et al. in view of Knight et al, or Mitelman et al., or Kleinjan et al., or Eppig et al., and further in view of Altshul et al.

Brosch et al reference teaches use of BAC library for comparative genomic studies. The library comprises about 5,000 BAC clones of known size. Sequences of termini of the clones is determined and used for either establishing BAC map of the parent genome, or for comparative genomic studies of other genomes. Thus, the end

sequence information of clones derived from *M. Tuberculosis* is used both for establishing a BAC map of genomic DNA from *M. Tuberculosis* (p. 2224), and for detection of differences with *M. bovis*. The latter identifies sequence differences which allow to estimate localization of polymorphisms. (p. 2226). The reference does not teach use of such end sequence profiling for genome analysis of individuals with a disease associated with chromosomal rearrangements

Roach et al. describe application of pairwise end sequencing to genomic mapping and sequencing. Pairs of sequences are derived from both ends of clones of known size. Use of pairwise strategies (using information of pair of sequences obtained from both sides of the clone) is shown to be beneficial for fine scale mapping, gene finding, and low- and high-pass sequencing. The reference does not teach use of such end sequence profiling for genome analysis of individuals with a disease associated with chromosomal rearrangements

Kelley et al describe end sequencing of BAC clones wherein library of BAC clones of known size is produced and sequence information from the termini of each clone is obtained (see abstract). The reference states that BAC library and the end sequence dataset are representative of the genome (p. 1545, right column). The reference does not teach using end sequence information of BAC clones to reveal difference between genomes of normal and diseased individuals.

The Brosch or Roach or Kelley references, although describing the method steps as claimed, does not teach use of such end sequence profiling for genome analysis of individuals with a disease associated with chromosomal rearrangements. However, it would be obvious to an artisan that the described technique demonstrated for bacterial genome analysis is applicable to comparative genomic studies of other genomes. The Brosch reference, itself, teaches that the BACs have a wide use for cloning DNA from various eucaryotic species (see p. 2221, second paragraph). Further, there are numerous reports describing chromosomal rearrangements emerging as an important cause of human genetic diseases. See, for example Knight et al, or Mitelman et al., or Kleinjan et al., or Eppig et al. (see abstracts). Thus, one skilled in the art would be motivated to apply a reliable and easy way of localizing genome changes, such as method of Brosch, to identify chromosomal rearrangement rearrangements which might be associated with genetically determined diseases.

As for computation methods for such comparative genomics studies, there are numerous available computational methods for nucleic acid sequence comparison, BLAST method (described in Alshtul et al) being the best known.

In regard to dependent claims, 2-6, 10-25, if there are any differences between Applicant's claimed methods and that of the prior art, the differences would be appear

minor in nature. Although the prior art do not teach all specifics of amount and density of clones (as in claims 6,15-18,19-22) or determining their frequency (as in claim 10,13,14), or determining steps (claims 24,25), or potential test/reference genome permutations (as in claims 3-5), or executing method using such tools as automated sequencing and computer (as in claims 22,23), it would be conventional and within the skill of the art to determine such parameters and usages as a part of routine optimization which is within the skill in the art to which this invention pertains.

Response to arguments

Applicant argues that the reference does not teach or suggest any use of terminal sequencing in genomic comparison. Contrary, however, the reference both describes comparison of genomes from different species (see abstract, p. 2221, last paragraph, and p. 2226), and use of sequence information on fragment termini in this comparison.

Further, applicants argue that the Brosch reference does not teach or suggest obtaining terminal sequence of clones. See, however, description of DNA sequence analysis, p. 2223-2224, and use of obtained sequence information in gene comparison on, p. 2226.

Prior art made of record

4. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: US Patents 5,830,645 and US 6,013,439.

Conclusion.

5. No claims are allowed

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

September 3, 2003

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

mlb